



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,628	06/01/2001	Cecil Yip	P04885US1	3027

7590

10/20/2003

Heidi S Nebel  
801 Grand Avenue Suite 3200  
Des Moines, IA 50309-2721

EXAMINER
----------

CLOW, LORI A

ART UNIT	PAPER NUMBER
----------	--------------

1631

17

DATE MAILED: 10/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/744,628

Applicant(s)

YIP ET AL.

Examiner

Lori A. Clow, Ph.D.

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 28 July 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 3-15 and 19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3-15 and 19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 15.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

Art Unit: 1631

### **DETAILED ACTION**

Applicants' arguments, filed 28 July 2003, have been fully considered by they are not deemed to be fully persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 3-15 and 19 are currently pending in the application.

Please note that the copy of amendment B, Paper No. 16, dated 28 July 2003 contains several black ink lines and marks making some of the claims and remarks difficult to read.

Please send a clean copy of this amendment with the response to this Office Action.

#### ***Claim Objections***

Claim 5 is objected to because of the following informalities: Claim 5 recites "an IR antagonist". Applicant is requested to define IR as "insulin receptor" the first time it is used in claim language. Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 112, 1<sup>st</sup> Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***New Matter***

Art Unit: 1631

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 19 recites the method of claim 3 wherein the fitted quaternary structure of insulin receptor is determined at a resolution of at least 3 Angstroms within the domains of the quaternary structure and at least 5 Angstroms between the domains of the quaternary structure. However, there is no apparent support in the specification for these limitations. Applicant is invited to point to specific page and line number in the specification for these limitations.

***Enablement***

Claims 3-6, 11-15, and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) and e) In order to practice the claimed invention one of skill in the art must be able to determine whether or not a compound modulates insulin receptor activity. However, the methods of claims 3-6, 11-15, and 19 are not enabled as the claims are lacking critical steps and information required for the performance of said methods. One of skill in the art would not be able to perform the invention as claimed and the steps as presently recited would not result in obtaining the desired information from the methods, i.e. prediction of modulators of insulin activity from a fitting method.

For example, in claim 3 and dependent claims, the method to supposedly determine a modulator of insulin activity comprises steps of comparing the structure of a compound to the fitted quaternary structure of the insulin receptor to determine if the compound interacts with the receptor. However, the steps end there. There is nothing that indicates whether or not some activity has occurred. The mere act of "fitting" does not in any way determine activity. Just because a compound may fit into a site on the insulin receptor does not mean that it will in any way have an effect on receptor activity. A simple comparison of structure to a compound would not yield any information regarding insulin receptor activity unless subsequent steps to test the fitting of the compound with the receptor were performed. The specification, at page 4, indicates that further steps are taken to determine activity. However, the steps of claim 3 do not recite these limitations and are therefore not enabled.

Claim 11 recites the further steps of providing a computer program on the computer, the computer program including structural coordinates defining a cam including at least one residue from the Cam-loop segment [...]. There is no indication or guidance in the specification about

Art Unit: 1631

the nature or meaning of a “cam”. As such, one of skill in the art would not know how to use this information to perform the steps of the invention.

One would look to the art to practice the invention. However, the art describes determining modulators of activity either by in vivo and in vitro assays or by computer simulation, as in the present invention. The prior art, however, provides specific steps that would lead one to identify modulators of activity. For example, the CAVEAT program (Lauri et al. Journal of Computer-Aided Molecular Design (1994) Vol. 8, pages 51-66) is described in great detail such that molecules and structures are analyzed by energy conformations, structures with patterns, steric interactions, rank, etc. such that mimics, or modulators may be determined. However, is not possible to practice said invention without undue experimentation due to the lack of method steps that would enable one to determine a modulator of activity from a mere comparison.

b) and c) The specification provides working examples of identifying modulators using computer simulation (page 59-60). However, claim 3 does not recite those steps.

d) The invention is drawn to determining modulators of the insulin receptor.

f) The skill of those in the art of pharmacogenomics is high.

g) The art is predictable if the proper method steps are employed.

h) The claims are broad because they are drawn to methods without sufficient steps to perform the methods. The skilled practitioner would first turn to the instant specification for guidance to practice the claimed methods. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art does not teach these methods. Finally, said

Art Unit: 1631

practitioner would turn to trial and error experimentation to determine the limits and steps required. Such represents undue experimentation.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-15 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-15 and 19 recite “derivative thereof” in reference to the fitted quaternary structure of the insulin receptor. It is unclear as to the metes and bounds of “derivative”. Does the derivative mean any modified insulin receptor? If the insulin receptor is modified is it still functional such that a modifier could be identified?

Claims 7-8 recite “the computer”. There is no antecedent basis in the claims for “the computer”.

Claims 7-8 refer to “approximate amino acid distances listed in Table 1”. However there are no such distances listed in Table 1. Only inter side chain distances are listed. Therefore, the limitation of the recited amino acid distances is unclear.

Claims 7-9 recite “display the quaternary structure thereof”. It is unclear as to what exactly is being displayed. Is the quaternary structure of the ligand binding site displayed?

Art Unit: 1631

Claims 11-14 are unclear in that they recite a "cam" and "a cam-loop segment". The specification does not define "cam" and it unclear as to what the cam refers. Is it a specific part of the ligand binding domain?

No claims are allowed.

### ***Inquiries***

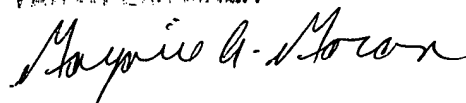
Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

**MARJORIE MORAN**  
**PATENT EXAMINER**



October 18, 2003

Lori A. Clow, Ph.D.

Art Unit 1631

